

Remarks

Regarding changes to the Claims:

The amendment to allowed claim 3 does not change the scope of the claim. The terms "genetic characteristic gene" and "trait-causing polymorphism" are equivalent. The terms "genetic characteristic" and "trait" are equivalent. (See definitions p. 11 lines 7-17.) The amendment is simply being made so that the usage of the terms "gene" and "polymorphism" in the claims is closer to the terms' usual usage.

The applicants respectfully request that the Examiner reconsider reinstated claim 102, formerly canceled claim 97. The applicants respectfully submit that several specific embodiments of the apparatus components with specific structural elements are described in the specification. For example: minisequencing on DNA arrays, dynamic allele-specific hybridization, microplate array diagonal gel electrophoresis, pyrosequencing, oligonucleotide-specific ligation, the TaqMan system and immobilized padlock probes (see p. 34 lines 15 to 18). Other specific embodiments are examples in endnotes VIII to XIII (p. 48). These include High Density DNA Arrays, immobilized sequence specific oligonucleotide probes and Elisa-based oligonucleotide ligation assay. (These endnotes and examples are cited on page 34 lines 5 to 14). In general, these examples use oligonucleotides and hybridization reactions. Some such reactions are for various types of amplification or to generate a physico-chemical signal, but the cited examples are not necessarily limited to these two categories. Another specific example is MALDITOF, which uses mass spectrometry. MALDITOF is cited on page 24 line 2 and in endnote I, page 48. The article cited in endnote I ("Weighing DNA for Fast Genetic Diagnosis") describes MALDITOF or an equivalent. In general mass spectrometry is used here to differentiate alleles based on mass and/or charge differences. But again the use of mass spectrometry is not necessarily limited to this description. A copy of the article on MALDITOF and several of the other articles in the endnotes (including articles on High Density DNA Arrays, immobilized sequence specific oligonucleotide probes and Elisa-based oligonucleotide ligation assay) were sent to the Examiner with the RCE submitted July 18, 2003 as new evidence of patentability. The applicants respectfully submit that the means of reinstated claim 102 are interpretable and searchable.

Some other points:

- 1) Some claims such as claim 138 refer to a CL-F region as "a collection of one or more CL-F points". This is supported by the specification, see p. 9 line 26 and p. 13 line 1.
- 2) Some claims such as claim 141 use a "mean χ^2_{tdt} calculation". The use of such a calculation to quantify increased power is described on page 42 lines 17 to 24 and also on page 166, last paragraph of the inventor's paper (Annals of Human Genetics (1998), 62, 159-179) which is incorporated by

reference into the patent application. (A copy of this paper was included with the IDS.) The actual equation, $\text{mean } \chi^2_{\text{tdt}} = 800(H/F) (2 P_t - 1)^2$, is also given on page 166, last paragraph of that paper.

3) Some claims such as claim 142 essentially refer to the "m/p ratio" departing from unity or " δ is not close to δ_{max} ". These concepts are supported by p. 6 lines 7 to 9 and p. 166 last paragraph of the inventor's paper (Annals of Human Genetics (1998), 62, 159-179).

4) Some claims such as claim 134 refer to "a gradient along the allele frequency dimension". Such a gradient is supported by p. 39 lines 3 to 7 and Table 2 (p. 40), p. 42 lines 14 and 15, as well as p. 24 line 29 to p. 25 line 4. Other support is found in Tables 1-3 in the inventor's paper.

5) Some changes and additions to the IDS have been made for the record (see accompanying amended IDS).

Conclusion

Twenty claims (3 independent, 17 singly dependent) have been favorably examined and allowed in a previous Office Action. These are claims 3-5, 8, 20, 21, 33-35, 38, 50, 51, 78-80, 83, 95 and new claims 99-101. Previously allowed claim 3 has been slightly amended.

Previously canceled independent claim 97 has been reinstated as independent claim 102 and new evidence of patentability was cited in the previously filed RCE and the Remarks section above. New claims 103 to 159 have been added. Some support for some of the new claims has been cited. An appropriate payment of the fee for the reinstated independent claim and new claims is enclosed. For the reasons advanced above, applicants respectfully submit that the application is now in condition for allowance and that action is earnestly solicited.

Respectfully submitted,



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